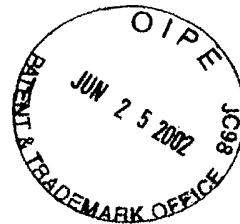


**Applicant:** Smith *et al.*      **Due Date:** None  
**Application No.:** 09/845,157      **Art Unit:** 1623  
**Filed:** May 1, 2001      **Examiner:** *To be assigned*  
**For:** Thermostable Reverse Transcriptases and Uses Thereof

When receipt stamp is placed hereon, the USPTO acknowledges receipt of the following documents:

1. SKGF Cover Letter;
2. First Supplemental Information Disclosure Statement;
3. List of cited references on Form PTO-1449 (15 sheets);
4. A copy of each reference cited on Form PTO-1449 (43 references); and
5. One (1) Return Postcard.



IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

In re application of:

Smith *et al.*

Appl. No. 09/845,157

Filed: May 1, 2001

For: **Thermostable Reverse  
Transcriptases and Uses Thereof**

Confirmation No. 2674

Art Unit: 1623

Examiner: *To be assigned*

Atty. Docket: 0942.5040001/RWE/MTT

**First Supplemental Information Disclosure Statement**

Commissioner for Patents  
Washington, D.C. 20231

Sir:

Listed on accompanying Form PTO-1449 are documents that may be considered material to the examination of this application, in compliance with the duty of disclosure requirements of 37 C.F.R. §§ 1.56, 1.97 and 1.98. A copy of each document is also provided.

Where the publication date of a listed document does not provide a month of publication, the year of publication of the listed document is sufficiently earlier than the effective U.S. filing date and any foreign priority date so that the month of publication is not in issue. Applicants have listed publication dates on the attached PTO-1449 based on information presently available to the undersigned. However, the listed publication dates should not be construed as an admission that the information was actually published on the date indicated.

Applicants reserve the right to establish the patentability of the claimed invention over any of the information provided herewith, and/or to prove that this information may not be prior art, and/or to prove that this information may not be enabling for the teachings purportedly offered. This statement should not be construed as a representation that a search

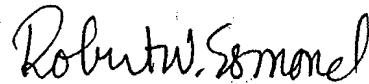
has been made, or that information more material to the examination of the present patent application does not exist.

This First Supplemental Information Disclosure Statement is being filed before the mailing date of a first Office Action on the merits. No statement or fee is required.

Consideration of the cited documents and making the same of record in the prosecution of the above-identified application is respectfully requested. The U.S. Patent and Trademark Office is hereby authorized to charge any fee deficiency, or credit any overpayment, to our Deposit Account No. 19-0036.

Respectfully submitted,

STERNE, KESSLER, GOLDSTEIN & FOX P.L.L.C.



Robert W. Esmond  
Attorney for Applicants  
Registration No. 32,893

Date: June 25, 2002

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FORM PTO-1449 <b>FIRST SUPPLEMENTAL INFORMATION DISCLOSURE STATEMENT</b>		ATTY. DOCKET NO. 0942.5040001/RWE/MTT	APPLICATION NO. 09/845,157
		APPLICANT Smith et al.	
		FILING DATE May 1, 2001	GROUP 1623

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	AM						Yes No
	AN						Yes No
	AO						Yes No
	AP						Yes No

**OTHER (Including Author, Title, Date, Pertinent Pages, etc.)**

	AR	1	Arnold, F.H., et al., "How enzymes adapt: lessons from directed evolution," <i>TRENDS Biochem. Sci.</i> 26:100-106, Elsevier Science Ltd. (February 2001)
	AS	1	Bailey, J.M., "Interpretation of Nitrocellulose Filter Assays of Protein-Nucleic Acid Binding," <i>Anal. Biochem.</i> 93:204-206, Academic Press, Inc. (1979)
	AT	1	Beard, W.A., et al., "Vertical-scanning Mutagenesis of a Critical Tryptophan in the Minor Groove Binding Track of HIV-1 Reverse Transcriptase. Molecular Nature of Polymerase-Nucleic Acid Interaction," <i>J. Biol. Chem.</i> 273:30435-30442, The American Society for Biochemistry and Molecular Biology, Inc. (1998)

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## OTHER (Including Author, Title, Date, Pertinent Pages, etc.)

AR	2	Bebenek, K., and Kunkel, T.A., "5. The Fidelity of Retroviral Reverse Transcriptases," in <i>Reverse Transcriptase</i> , Skalka, A.M. and Goff, S.P., eds., Cold Spring Harbor Laboratory Press, Plainview, New York, pp. 85-102 (1993)
AS	2	Bebenek, K., et al., "A minor groove binding track in reverse transcriptase," <i>Nat. Struct. Biol.</i> 4:194-197, Nature Publishing Co. (1997)
AT	2	Cadwell, R.C., and Joyce, G.F., "Randomization of Genes by PCR Mutagenesis," <i>PCR Meth. Appl.</i> 2:28-33, Cold Spring Harbor Laboratory Press (1992)

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	AR	3	Cambillau, C., and Claverie, J.-M., "Structural and Genomic Correlates of Hyperthermostability," <i>J. Biol. Chem.</i> 275:32383-32386, The American Society for Biochemistry and Molecular Biology, Inc. (October 2000)
	AS	3	D'Alessio, J.M., and Gerard, G.F., "Second-strand cDNA synthesis with <i>E. coli</i> DNA polymerase I and RNase H: the fate of information at the mRNA 5' terminus and the effect of <i>E. coli</i> DNA ligase," <i>Nucl. Acids Res.</i> 16:1999-2014, IRL Press Ltd. (1988)
	AT	3	DeStefano, J.J., et al., "Polymerization and RNase H Activities of the Reverse Transcriptases from Avian Myeloblastosis, Human Immunodeficiency, and Moloney Murine Leukemia Viruses Are Functionally Uncoupled," <i>J. Biol. Chem.</i> 266:7423-7431, The American Society for Biochemistry and Molecular Biology, Inc. (1991)

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	AR	4	DeStefano, J.J., et al., "Characterization of an RNase H deficient mutant of human immunodeficiency virus-1 reverse transcriptase having an aspartate to asparagine change at position 498," <i>Biochim. Biophys. Acta</i> 1219:380-388, Elsevier Science B.V. (1994)
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	AT	4	Georgiadis, M.M., et al., "Mechanistic implications from the structure of a catalytic fragment of Moloney murine leukemia virus reverse transcriptase," <i>Structure</i> 3:879-892, Current Biology Ltd. (1995)

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AR	5	Gerard, G.F., et al., "Poly(2'-O-methylcytidylate) Oligodeoxyguanylate as a Template for the Ribonucleic Acid Directed Deoxyribonucleic Acid Polymerase in Ribonucleic Acid Tumor Virus Particles and a Specific Probe for the Ribonucleic Acid Directed Enzyme in Transformed Murine Cells," <i>Biochem.</i> 13:1632-1641, The American Chemical Society (1974)
AS	5	Gerard, G.F., and D'Alessio, J.M., "Reverse Transcriptase (EC 2.7.7.49). The Use of Cloned Moloney Murine Leukemia Virus Reverse Transcriptase to Synthesize DNA from RNA," in <i>Methods in Molecular Biology</i> , Volume 16: <i>Enzymes of Molecular Biology</i> , Burrell, M.M., ed., Humana Press, Totowa, NJ, pp.73-93 (1993)
AT	5	Gerard, G.F., et al., "Reverse Transcriptase. The Use of Cloned Moloney Murine Leukemia Virus Reverse Transcriptase to Synthesize DNA from RNA," <i>Mol. Biotechnol.</i> 8:61-77, Humana Press (1997)

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## OTHER (Including Author, Title, Date, Pertinent Pages, etc.)

	AR	6	Harrison, G.P., et al., "Pausing of reverse transcriptase on retroviral RNA templates is influenced by secondary structures both 5' and 3' of the catalytic site," <i>Nucl. Acids Res.</i> 26:3433-3442, Oxford University Press (1998)
	AS	6	Houts, G.E., et al., "Reverse Transcriptase from Avian Myeloblastosis Virus," <i>J. Virol.</i> 29:517-522, American Society for Microbiology (1979)
	AT	6	Huang, H., et al., "Structure of a Covalently Trapped Catalytic Complex of HIV-1 Reverse Transcriptase: Implications for Drug Resistance," <i>Science</i> 282:1669-1675, American Association for the Advancement of Science (1998)

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## OTHER (Including Author, Title, Date, Pertinent Pages, etc.)

	AR	7	Jacobo-Molina, A., et al., "Crystal structure of human immunodeficiency virus type 1 reverse transcriptase complexed with double-stranded DNA at 3.0 Å resolution shows bent DNA," Proc. Natl. Acad. Sci. (USA) 90:6320-6324, National Academy of Sciences of the USA (1993)
	AS	7	Kohlstaedt, L.A., et al., "Crystal Structure at 3.5 Å Resolution of HIV-1 Reverse Transcriptase Complexed with an Inhibitor," Science 256:1783-1790, American Association for the Advancement of Science (1992)
	AT	7	Kotewicz, M.L., et al., "Isolation of cloned Moloney murine leukemia virus reverse transcriptase lacking ribonuclease H activity," Nucl. Acids Res. 16:265-277, IRL Press Ltd. (1988)

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	AR	8	Kneller, D.G., et al., "Improvements in Protein Secondary Structure Prediction by An Enhanced Neural Network," <i>J. Mol. Biol.</i> 214:171-182, Academic Press Ltd. (1990)
	AS	8	Krug, M.S., and Berger, S.L., "[33] First-Strand cDNA Synthesis Primed with Oligo(dT)," <i>Meth. Enzymol.</i> 152:316-325, Academic Press, Inc. (1987)
	AT	8	Kumar, S., and Nussinov, R., "How do thermophilic proteins deal with heat?" <i>Cell. Mol. Life Sci.</i> 58:1216-1233, Birkhauser Verlag (August 2001)

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	AP						Yes No

## OTHER (Including Author, Title, Date, Pertinent Pages, etc.)

	AR	9	Kunkel, T.A., et al., "[19] Rapid and Efficient Site-Specific Mutagenesis without Phenotypic Selection," <i>Meth. Enzymol.</i> 154:367-383, Academic Press, Inc. (1987)
	AS	9	Kunkel, T.A., et al., "[6] Efficient Site-Directed Mutagenesis Using Uracil-Containing DNA," <i>Meth. Enzymol.</i> 204:125-139, Academic Press, Inc. (1991)
	AT	9	Le Grice, S.F.J., "9. Human Immunodeficiency Virus Reverse Transcriptase," in <i>Reverse Transcriptase</i> , Skalka, A.M. and Goff, S.P., eds., Cold Spring Harbor Laboratory Press, Plainview, NY, pp. 163-191 (1993)

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## OTHER (Including Author, Title, Date, Pertinent Pages, etc.)

AR	<u>10</u>	Lehmann, M., and Wyss, M., "Engineering proteins for thermostability: the use of sequence alignments versus rational design and directed evolution," <i>Curr. Opin. Biotechnol.</i> 12:371-375, Elsevier Science Ltd. (August 2001)
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AT	<u>10</u>	McDonell, M.W., et al., "Analysis of Restriction Fragments of T7 DNA and Determination of Molecular Weights by Electrophoresis in Neutral and Alkaline Gels," <i>J. Mol. Biol.</i> 110:119-146, Academic Press, Inc. (1977)

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	AR	11	Mölling, K., et al., "Association of Viral Reverse Transcriptase with an Enzyme degrading the RNA Moiety of RNA-DNA Hybrids," <i>Nature New Biology</i> 234:240-243, Macmillan Journals Ltd. (1971)
	AS	11	Myers, T.W., and Gelfand, D.H., "Reverse Transcription and DNA Amplification by a <i>Thermus thermophilus</i> DNA Polymerase," <i>Biochem</i> 30:7661-7666, The American Chemical Society (1991)
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	AR	<u>12</u>	Prasad, V.R., "8. Genetic Analysis of Retroviral Reverse Transcriptase Structure and Function," in Reverse Transcriptase, Skalka, A.M. and Goff, S.P., eds., Cold Spring Harbor Laboratory Press, Plainview, NY, pp. 135-162 (1993)
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	AP						Yes No

## OTHER (Including Author, Title, Date, Pertinent Pages, etc.)

AR	<u>13</u>	Skalka, A.M., "10. Endonuclease Activity Associated with Reverse Transcriptase of Avian Sarcoma-Leukosis Viruses," in <i>Reverse Transcriptase</i> , Skalka, A.M. and Goff, S.P., eds., Cold Spring Harbor Laboratory Press, Plainview, NY, pp. 193-204 (1993).
AS	<u>13</u>	Stemmer, W.P.C., "Rapid evolution of a protein <i>in vitro</i> by DNA shuffling," <i>Nature</i> 370:389-391, Macmillan Journals Ltd. (1994)
AT	<u>13</u>	Strauss, H.S., et al., "Variables affecting the selectivity and efficiency of retention of DNA fragments by <i>E. coli</i> RNA polymerase in the nitrocellulose-filter-binding assay," <i>Gene</i> 13:75-87, Elsevier/North-Holland Biomedical Press (1981)

EXAMINER

DATE CONSIDERED

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FORM PTO-1449  <u>FIRST SUPPLEMENTAL INFORMATION DISCLOSURE STATEMENT</u>		ATTY. DOCKET NO. 0942.5040001/RWE/MTT	APPLICATION NO. 09/845,157
		APPLICANT Smith et al.	
		FILING DATE May 1, 2001	GROUP 1623

U. S. PATENT DOCUMENTS							
EXAMINER INITIAL		DOCUMENT NUMBER	DATE	NAME	CLASS	SUB-CLASS	FILING DATE
	AA						
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## FOREIGN PATENT DOCUMENTS

EXAMINER INITIAL		DOCUMENT NUMBER	DATE	COUNTRY	CLASS	SUB-CLASS	TRANSLATION
	AL						Yes No
	AM						Yes No
	AN						Yes No
	AO						Yes No
	AP						Yes No

## OTHER (Including Author, Title, Date, Pertinent Pages, etc.)

	AR	<u>14</u>	Tosh, C., et al., "One-Tube and One-Buffer System of RT-PCR Amplification of 1D Gene of Foot-and-Mouth Disease Virus Field Isolates," <i>Acta Virol.</i> 41:153-155, Slovak Academic Press (1997)
	AS	<u>14</u>	Verma, I., et al., "Studies on Reverse Transcriptase of RNA Tumor Viruses. III. Properties of Purified Moloney Murine Leukemia Virus DNA Polymerase and Associated RNase H," <i>J. Virol.</i> 15:843-854, American Society for Microbiology (1975)
	AT	<u>14</u>	Wells, J.A., "Additivity of Mutational Effects in Proteins," <i>Biochem.</i> 29:8509-8517, The American Chemical Society (1990)

EXAMINER	DATE CONSIDERED
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	AL						Yes No
	AM						Yes No
	AN						Yes No
	AO						Yes No
	AP						Yes No

## OTHER (Including Author, Title, Date, Pertinent Pages, etc.)

	AR	15	Wu, W., et al., "Human Immunodeficiency Virus Type 1 Nucleocapsid Protein Reduces Reverse Transcriptase Pausing at a Secondary Structure near the Murine Leukemia Virus Polypurine Tract," J. Virol. 70:7132-7142, American Society for Microbiology (1996)
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	AT		

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